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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,494	05/08/2001	Ehud Goldin	3394/1H557US1	2229

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EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/851,494	GOLDIN ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *8-32 and 36-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1) Claims 1 to 38 are pending in the instant application.

2) Claims 8 to 32 and 36 to 38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the correspondence filed 29 September of 2003. The traversal is on the ground(s) that a search of the inventions of Groups I, IV and V in a single application would not pose an undue burden. This is not found persuasive because M.P.E.P. 803 states that:

> " For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. That prima facie showing may be rebutted by appropriate showings or evidence by the applicant."

Serious burden was shown in the original requirement by the separate classification and separate status in the art of the different inventions. Applicant has provided neither a showing nor evidence to the contrary. Further, the three inventions referred to by Applicant are unrelated. Neither the diagnostic process of invention IV nor the kit of invention V produces or uses the nucleic acid of invention I. Therefore, 37 C.F.R. § 1.141(b) is not applicable to the instant requirement.

The requirement is still deemed proper and is therefore made FINAL.

3) The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate

paper." Therefore, unless the references have been cited by the examiner on a form PTO-892, they have not been considered.

4) The following references are being cited by the examiner as relevant to the instant invention;

Sun et al. "Mucolipidosis type IV is caused by mutations in a gene encoding a novel transient receptor potential channel." *Human Molecular Genetics* Vol. 9(17):2471-2478, Sept. 2000,

Bargal et al. "Identification of the gene causing mucolipidosis type IV." Nature Genetics Vol. 26:120-123, Sept. 2000.

Bassi et al."Cloning of the gene encoding a novel integral membrane protein, Mucolipidin-and identification of the two major founder mutations causing mucolipidosis type IV." *American Journal of Human Genetics* Vol. 67:1110-1120, 2000.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5) Claims 1 to 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The instant specification discloses that all of the nucleotide sequences referred to in these claims were found in human subjects. Therefore, these claims encompass nucleic acids as they occur in nature.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6) Claims 1, 2, and 4 to 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims encompass

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the genus of nucleic acids encompassed by the instant claims. These claims appear to encompass the genus of nucleic acids defined by the limitations "encoding a MCOLN1 polypeptide" encoded by "a *MCOLN1* gene" having a mutation that "results in a defect in expression of a functional MCOLN1", and having at least 95% sequence identity to SEQ ID NO:1 or 2. The structural nature of the mutation that "results in a defect in expression of a functional MCOLN1" is not specified and one of ordinary skill in the art of molecular biology would not reasonably conclude, upon viewing the evidence of record, that any deviation from the nucleotide sequence presented in SEQ ID NO:1 or 2 will result in the required functional defect. Therefore, the functional limitation recited in the claims does not inherently result from the structural limitations recited therein.

Table 1 on page 53 of the instant specification and the text on pages 52 to 54 therein describe specific "mutations" in the "MCOLN1" gene, relative to a single wild-type "MCOLN1" sequence presented in SEQ ID NO:1 and 2, which are found in individuals which had been physiologically shown to be predisposed to mucolipidosis and in which the type of mutation detected would account for a functional defect in the protein encoded thereby. This evidence clearly supports a conclusion that the specific mutations described in the instant specification are diagnostic for a predisposition to mucolipidosis.

However, the instant specification is silent on variations in "MCOLN1" gene sequences among the control individuals. It does not deny that such variations exist, it simply does not discuss them. The "MCOLN1" sequence presented in the instant specification is 580 amino acids in length. It is well known in the art of molecular that nucleotide sequences encoding an amino acid sequence of any particular protein will have inconsequential differences from individual to individual, as will the amino acid sequence encoded thereby. This is why all humans are not identical and why DNA fingerprinting works. In the absence of evidence to the contrary, an artisan of ordinary skill would find it difficult to believe that the amino acid sequence of "MCOLN1" does not vary at even a single amino acid residue from SEQ ID NO:3 within the population of humans not predisposed to mucolipidosis.. Given the polymorphic nature of the different forms of "MOCLN1" genetic defects which are associated with mucolipidosis, including those that result "high" expression, decreased expression or normal expression levels of the encoded product, as described on page 54 of the instant specification, an artisan would reasonable expect to find an equally polymorphic assortment of "MOCLN1" gene sequence variations having inconsequential differences between themselves and SEQ ID NO:2 of the instant specification within a "normal" population of humans.

Whereas the instant specification describes a number of very specific genetic defects in the human *MOCLN1* gene which are clearly useful in the identification of individuals carrying such genes, it does not provide a general structural formula that defines the claimed genus of nucleic acids. In the decision of *The Regents of the*

University of California v. Eli Lilly and Company, 43 USPQ2d 1398 (CAFC 1997), the court held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Whereas the instant specification provides a detailed description of a number of isolated DNAs encoding particular human *MOCLN1* genes having very specific physical and structural properties, the instant specification does not provide a structural formula which is definitive of all human *MOCLN1* genes having a mutation that "results in a defect in expression of a functional MCOLN1". Whereas the instant specification may

identify some properties which are common to the human *MOCLN1* genes that are disclosed in the instant specification, it does not identify those defining structural elements which provide the unique structural properties of all human *MOCLN1* genes having a mutation that "results in a defect in expression of a functional MCOLN1". Because one of ordinary skill would expect the "MCOLN1" gene to vary in minor and inconsequential ways from individual to individual, one would not expect the discovery of a "MCOLN1" gene, in an individual, which varies from SEQ ID NO:1 OR 2 of the instant specification in any way to be diagnostic for a predisposition to mucolipidosis. If Applicant is aware of any evidence that the sequence of the "MOCLN1" gene is invariant from individual to individual within that portion of the human population not showing a predisposition to mucolipidosis then they are encouraged to make that evidence of record. Otherwise, the evidence currently of record supports the instant rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7) Claims 1 to 7 and 33 to 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7.1) Claims 1 to 7 are confusing because it is unclear if the claimed nucleic acid is required to contain a mutation. Claims 2 to 4 appear to require a mutation whereas claims 6 and 7 do not. Clarification is required.

7.2) Claims 1 to 7 and 33 to 35 are vague and indefinite in so far as they employ the term "MCOLN1" as a limitation. Because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "MCOLN1" an artisan can not determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation. For example, the text on pages 6 and 7 of the instant specification states that " MCOLN1 functions include, but are not limited to, HCl secretion, ion channel activity, and secretion of solutes from intracellular vesicles" and that "[o]ther MCOLN1 functions include, but are not limited to, binding with MCOLN 1-specific antibodies". It is unclear what specific functions define and distinguish "MCOL1" from other, structurally or functionally related proteins since the logic of defining a "MCOL1" protein by its ability to bind to "MCOLN l-specific antibodies" is circular.

7.3) Claims 1 to 7 and 33 to 35 are vague and indefinite in so far as they employ the limitation "at least about 95% identical". The text on page 7 of the instant specification states that "[i]n a specific embodiment, the term "about" or "approximately" means within 20%, preferably within 10%, and more preferably within 5% of a given value or range". Because the definition of "about" as provided of page 7 of the instant specification is particularly vague and indefinite, it is not possible to determine the metes and bounds of a claim employing this limitation.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8) Claims 1, 5 to 7 and 33 to 35 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by the Curtis et al. publication (Pub. No. US 2002/0035056 A1) and the Lal et al. publication (Pub. No. US 2002/0182671 A1). The amino acid sequence presented in SEQ ID NO:3 of the instant application is identical to the amino acid sequence presented in SEQ ID NO:2 of Curtis et al. and SEQ ID NO:13 of Lal et al. Each of these publication described an isolated nucleic acid encoding a protein comprising that sequence, as well as a vector and host cell comprising that nucleic acid. Curtis et al. Has an effective filing date under 35 U.S.C. 119(e) of 07 April of 2000 and Lal et al. has an effective filing date under 35 U.S.C. 119(e) of 17 August of 1999.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242 or (703) 872-9306. Official responses under 37 C.F.R. § 1.116 should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN ULM
PRIMARY EXAMINER
GROUP 1600